

A hearing was held on October 21, 2004. Testifying for petitioner were Dr. Michael Heifets and Thomas E. Stewart. Testifying for respondent was Dr. Michael Gottlieb.

FACTS

Petitioner was born on May 22, 1954. He received his first hepatitis B vaccination on August 10, 2000. He received his second hepatitis B vaccination on September 13, 2000.² Med. recs. at Ex. 3, pp. 1, 3.

Three months later, on December 8, 2000, petitioner went to an emergency room at Virtua Health, Memorial Hospital of Burlington County, complaining that, starting about two and one-half days previously, he had precordial (in front of the heart; involving the precordium)³ discomfort lasting a couple of hours. One and one-half days previously, he had dyspnea (difficult or labored

within the banned categories listed above, the special master shall delete such material from public access.

² In petitioner's affidavit, dated August 5, 2003, he states that, within several weeks of his second hepatitis B vaccination, he "began to experience severe pains in my stomach. The pains would last for 20-30 seconds then subside, 20-45 minutes later they would come again. This continued for several weeks." Ex. 2, p. 2. He continues that, shortly after the stomach pains began, he began urinating froth. Ex. 2, pp. 2-3. Then, several days later, his legs swelled up and, the following day, his legs were so swollen, he had no ankles. Ex. 2, p. 3. He called his cousin who is a registered nurse. His family had a history of heart attacks, and he was feeling lightheaded and dizzy. *Id.* He went to the hospital to find out what was going on. *Id.* In a supplemental affidavit, dated without a specific date in January 2004, petitioner states that he does not know how long after the second hepatitis B vaccination, the frothing began. Second Vol. IV, Ex. 3, pp. 1-2. When he got to the hospital, he was so nervous, he did not give anyone a history of the stomach pains or urine froth because he thought he was having a heart attack. Second Vol. IV, Ex. 3, p. 2. He reasserts that his symptoms of nephrotic syndrome came "just weeks" after the second hepatitis B vaccination, but he does not know how long was the interval between the second vaccination and the frothing of his urine. Second Vol. IV, Ex. 3, p. 3.

³ <http://www.wordreference.com/definition/precordial>.

respiration).⁴ That night, he had swelling of his lower extremities. He discussed this with a relative who is a nurse and she asked him if he were experiencing other symptoms, such as lightheadedness. After speaking with her, petitioner began experiencing lightheadedness and a vague feeling of discomfort and tingling. Med. recs. at Ex. 4, p. 6.

He was admitted to Virtua Health, Memorial Hospital of Burlington County, on December 9, 2000, saying he noted increasing swelling of his lower extremities and, last evening (December 8, 2000), he had an episode of lightheadedness with chest discomfort. Med. recs. at Ex. 4, p. 8. He had a history of asthma and noted swelling of his lower extremities over the last several days. Med. recs. at Ex. 4, pp. 6, 8; Vol. II, part 1, p. 8. He stated there was no history of similar problems in the past. Med. recs. at Ex. 4, p. 8; Vol. II, part 1, p. 10. He denied diarrhea, constipation, flatulence, arthralgia, and myalgias. Id. Petitioner was dismissed from the hospital on the same day. Med. recs. at Ex. 4, p. 11; Vol. II, part 1, p. 17.

For Virtua Health, Memorial Hospital of Burlington County's patient admission database, a physician's assistant filled out a questionnaire about petitioner's prior and current health on December 9, 2000. Med. recs. at Vol. II, part 1, p. 18. In answer to the question if he were having acute pain now, the answer was no. The question if he had recurrent pain in recent weeks or months was unanswered. Med. recs. at Vol. II, part 1, p. 19. In answer to the question if he were having chronic pain, the answer was no. Id. In answer to the genitourinary questions, including whether petitioner's urine was clear, the answer checked was that he was within normal. Med. recs. at Vol. II, part 1, p. 21. In answer to the question of edema, the PA wrote +1 edema bilaterally in petitioner's lower extremities. Id.; see also part 1, p. 20.

⁴ <http://www.wordreference.com/definition/dyspnea.htm?v=b>.

Further, in the records for December 9, 2000, petitioner denied he had any pain at that time. Med. recs. at Vol. II, part 1, p. 32. For the section devoted to genitourinary symptoms, including clear urine, the box for within normal was checked. Med. recs. at Vol. II, part 1, pp. 33, 39.

On December 14, 2000, petitioner saw Dr. Michael Heifets, a nephrologist, as a referral from petitioner's family practitioner, Dr. John Scappaticci, DO. Petitioner told Dr. Heifets that he had noted progressive increase in peripheral edema and weight gain over the last several weeks, as well as the appearance of suds in his urine several weeks ago. Med. recs. at Ex. 7, p. 17. The prior week, he felt lightheaded and had shortness of breath. At Memorial Hospital, petitioner was found to have significant proteinuria. Petitioner had no past history of kidney disease, hematuria, dysuria, or abnormal urine appearance. He also had no history of stones or flank pain. Id. He had abnormal liver tests over 15 years ago. Id.

Petitioner's major complaint to Dr. Heifets was peripheral edema. His shortness of breath was associated with the increase in edema and fluid retention. Med. recs. at Ex. 7, p. 18. He had received two hepatitis B vaccinations with the last injection approximately two and one-half months ago. Id. Whereas in Memorial Hospital emergency room on December 8, 2000, petitioner had +1 edema (Ex. 4, p. 7) and, upon hospital admission on December 9, 2000, he had +2 edema (Ex. 4, p. 8), Dr. Heifets found +3 edema in the lower extremities on December 13, 2000 (Ex. 7, p. 18).

Dr. Heifets' impression was "acute onset of nephrotic syndrome with exaggeration of hyperlipidemia. At this point, it is unclear what the etiology is of his nephrotic syndrome." Med. recs. at Ex. 7, p. 8. Petitioner's fluid overload was secondary to his nephrotic syndrome. Id.

From December 28 to 30, 2000, petitioner was in Virtua Health, Memorial Hospital of Burlington County, because of refractory edema. He responded quickly to Lasix and Zaroxolyn

intravenous treatment with an 11-pound weight loss in the first day. Med. recs. at Ex. 8, p. 2. The history recorded by Dr. Heifets was that Mr. Stewart had progressive edema, difficulty walking, and rapid weight gain in spite of increasing doses of diuretics. He is a policeman who was in his usual state of health until early December, when he noticed progressive increase in peripheral edema and leg swelling. His urine became foamy approximately two weeks ago (i.e., mid-December 2000) and looked like soapsuds. He denied flank pain. He had an episode of lightheadedness and shortness of breath two to three weeks ago. He had no past history of systemic illness. Med. recs. at Ex. 8, p. 4.

Petitioner told Dr. Heifets he noticed some increase in abdominal girth over the last several weeks. Med. recs. at Ex. 8, pp. 4-5. Over the last two days, he had difficulty walking because of severe edema. His weight had increased from 290 pounds on December 14, 2000, to 302 pounds on December 28, 2000. Petitioner had 4+ edema in his lower extremities. Med. recs. at Ex. 8, p. 5. According to Dr. Scappaticci's office, hepatitis B surface antigen was negative. Med. recs. at Ex. 8, p. 6. At the time, Dr. Heifets wrote in the medical records: "I am somewhat puzzled about the association of the onset of nephrotic syndrome and the recent hepatitis B vaccination. I am not aware of any episodes documenting causality between the two although this possibility should be entertained as well." Med. recs. at Ex. 8, p. 7.

On December 29, 2000, Dr. William L. Niedrach was called in as a consultant. Petitioner stated he had no previous urologic history except for a vasectomy. Med. recs. at Ex. 8, p. 9. An MRI was consistent with a 3 cm. right renal cyst consistent with a benign cyst. Med. recs. at Ex. 8, p. 10.

On January 18, 2001, petitioner saw Dr. Heifets, complaining of severe cramping which did not subside. Med. recs. at Ex. 7, p. 13. By stopping medications, Dr. Heifets succeeded in ending the cramping. Id. Petitioner's volume overload and peripheral edema were starting to improve three weeks after starting steroid treatment, but he had abnormal liver function tests. Id.

On February 23, 2001, petitioner's nephrotic syndrome appeared to enter remission after six weeks of prednisone. Med. recs. at Ex. 7, p. 12. On March 20, 2001, petitioner's nephrotic syndrome completely resolved after two months on prednisone. Med. recs. at Ex. 7, p. 11.

On March 20, 2001, Dr. Heifets wrote a letter to petitioner's former counsel, stating he first saw petitioner on December 14, 2000, who "presented then with very recent onset of increasing swelling in the lower extremities, shortness of breath, and was found to have significant fluid overload." Med. recs. at Ex. 7, p. 9. The significant fluid overload was due to severe protein leakage from the kidneys into the urine. Id. Numerous laboratory tests were performed to look for the cause of his kidney impairment. The tests indicated no underlying chronic disease could be the primary cause for his kidney condition. Id. The possible cause for petitioner's condition is minimal change disease also known as nil disease as well as lipoid nephrosis. Med. recs. at Ex. 7, p. 10. Petitioner told him he had received hepatitis B vaccine in the fall of 2000 which preceded onset of his kidney symptoms. He did not have any febrile illnesses or infections of the ears, nose, and throat or other significant illnesses preceding the onset of his symptoms of fluid overload. Med. recs. at Ex. 7, p. 9. "Given the time sequence, it is more likely than not that hepatitis B vaccination could have triggered immune reaction in his body. This, in turn, resulted in protein leak in the kidneys and nephrotic syndrome." Med. recs. at Ex. 7, p. 10.

On October 4, 2001, petitioner saw Dr. David C. Lee, a neurologist, on referral from Dr. Heifets. Starting in July, he had severe burning in his legs and feet, causing him to be unable to work. Med. recs. at Ex. 9, p. 3. His neurological examination was normal. He had residual edema in the legs up to the mid-shin area. The remainder of the examination was normal and non-focal. Med. recs. at Ex. 9, p. 4. Dr. Lee diagnosed petitioner with peripheral neuropathy, probably as a combination of his nephrotic syndrome, edema, and multiple medications. Id. Nerve conduction and EMG studies were performed on October 31, 2001, which showed mild sensorimotor peripheral neuropathy. Med. recs. at Ex. 9, pp. 6-7. Dr. Lee opined that petitioner should make a spontaneous recovery because the findings were quite mild. Med. recs. at Ex. 9, p. 2.

Petitioner saw Dr. Lee again on December 19, 2001. He had returned to work, but had 2+ edema of his bilateral extremities extending to mid-shin. Med. recs. at Ex. 9, p. 1.

From January 14 to 15, 2002, petitioner was in Virtua Health, Memorial Hospital of Burlington County. Med. recs. at Vol. II, part 3, p. 1. Petitioner's past history was nephrotic syndrome in December 2000. Med. recs. at Vol. II, part 3, p. 4. A renal biopsy on January 14, 2002 showed a complex cystic lesion versus solid lesion in the right kidney. Med. recs. at Vol. II, part 3, p. 23.

A renal biopsy report dated January 16, 2002 (the specimen was received January 15, 2002), concludes that petitioner has minimal change disease. Med. recs. at Vol. VII, p. 2. Thirteen glomeruli (small intertwined groups of capillaries)⁵ were identified, none of which was segmentally

⁵ <http://www.wordreference.com/definition/glomerulus.htm?v=b>

or globally sclerotic. There was mild swelling of the podocytes.⁶ Med. recs. at Vol. VII, p. 1. The immunofluorescence findings of 1+ segmental granular mesangial positivity for IgM support the diagnosis of minimal change disease and provide evidence against glomerular disease of the immune complex type. Med. recs. at Vol. VII, p. 2. One of three glomeruli sampled for electron microscopy was globally sclerotic. The major findings are diffuse podocyte hypertrophy with extensive foot process effacement involving approximately 90% of the glomerular capillary surface area, accompanied by focal microvillous transformation. The results were minimal change disease with 90% foot process fusion. Med. recs. at Vol. VII, p. 3.

On July 15, 2002, Dr. Steven Klein, a DO who evaluates disability, wrote that petitioner's nephrotic syndrome occurred several weeks after his hepatitis B vaccinations and was a direct result of them, and he had no other risk factors for nephrotic syndrome. Med. recs. at Ex. 11, p. 4.

Dr. David S. Share replaced Dr. Heifets in his nephrologic care on November 19, 2002. Med. recs. at Vol. III, p. 7. Dr. Share opined petitioner might have progressed from renal change disease to focal segmental glomerulosclerosis (FSGS). Or he might have a very difficult case of steroid-dependent minimal change disease. He had minimal microscopic hematuria, which he did not have previously, which would be consistent with a conversion to FSGS. Id.

Dr. Share saw petitioner on May 2, 2003, and stated he was doing beautifully. His nephrotic syndrome was in remission. Med. recs. at Vol. III, p. 1.

⁶ Podocyte is "a modified epithelial cell of the visceral layer ... of the renal glomerulus, having a small perikaryon and a number of primary and secondary footlike radiating processes ... which interdigitate with those of other podocytes and which embrace the basal lamina of glomerular capillaries." Dorland's Illustrated Medical Dictionary, 27th Ed. (1988), at 1322.

On November 18, 2003, Dr. Heifets wrote a letter to petitioner's current counsel, stating that petitioner was seen for progressive edema of his lower extremities and fluid overload in late fall/early winter of 2000. The only significant event preceding his diagnosis of nephrotic syndrome by several weeks was hepatitis B vaccination. Med. recs. at Vol. IV, p. 1. "Based on the sequence of events, it is more likely than not, that hepatitis B vaccination precipitated nephrotic syndrome in Mr. Stewart's case." Med. recs. at Vol. IV, p. 1.

On January 12, 2004, Dr. Heifets wrote another letter to petitioner's current counsel, stating:

The duration of time between exposure to Hepatitis B vaccine and onset of symptoms could be many weeks, if not months. Nephrotic syndrome and minimal change neuropathy of Mr. Stewart, as well as many other immunologically mediated kidney diseases (for example allergic interstitial nephritis) may become manifest a long time after the exposure to offending agent. The reason being is that the exposure triggers a "[sic] silent immunologic process, which takes time to exert substantial damage to the kidney structure to produce clinically visible and detectable clinical disease, such as heavy proteinuria in Mr. Stewart's case. For example, proteinuria (protein leak into the urine) would start at a low level, and proceed to initiate overall bodily response, such as edema, etc, at very low level initially and only after proteinuria reaches heavy amounts and is present for a sufficient time, patient will then develop symptoms and signs of clinically detectable nephrotic syndrome.

Thus, usually, the onset of actual condition and its manifestation and detection could be separated by many weeks and months. Based on my clinical experience and knowledge, review of medical literature and Mr. Stewart's records, I can state with certainty that his nephrotic syndrome was within a reasonable degree of medical probability caused by hepatitis B vaccination.

Med. recs. at a second Vol. IV, Ex, 1, p. 1; see also Vol. V, Ex. 1, p. 1.

Other Submitted Material

Petitioner filed as Vol. V, Ex. 2, three articles. The first is a letter entitled "Nephrotic syndrome associated with recombinant hepatitis B vaccination: a causal relationship or just a mere association?" by S. Ozdemir, et al., 13 *Nephrol Dialysis and Transplantation* 1888-89 (1998). They

report the case of a three-year-old boy with a four-day history of swelling of the eyelids 17 days after his second hepatitis B vaccination. Vol. V, Ex. 2, p. 1.

The second is an article entitled “Nephrotic syndrome following hepatitis B vaccination,” by I. Islek and M. Cakir, 14 *Ped Nephrol* 89-90 (2000). They report the case of a four-year-old boy with swelling of the eyelids 8 days after receiving his third hepatitis B vaccination. He was diagnosed with nephrotic syndrome due to hepatitis B vaccine. The authors suggest that the timing of the minimal change nephrotic syndrome after recombinant hepatitis B vaccination strongly favors an immune-mediated side effect of the vaccination. Vol. V, Ex. 2, p. 3.

The third is a letter entitled, “Nephrotic syndrome after recombinant hepatitis B vaccine,” by F. Mocario, et al., 45 *Clin Nephrol* 5: 349 (1995). The authors describe the case of a 40-year-old nurse who was admitted to the hospital with an overt nephrotic syndrome (generalized edema, heavy proteinuria) after the second hepatitis B vaccination. They do not state the onset interval. Vol. V, Ex. 2, p. 6.

Petitioner filed as Vol. VIII one textbook chapter and four articles. The first is a chapter from the 14th edition of Harrison’s Principles of Internal Medicine, pp. 1540-41 (“Nephrotic Syndrome”). The key component of nephrotic syndrome is proteinuria, resulting from altered permeability of the glomerular filtration barrier for protein. Id. at 1540. Six entities account for 90% of cases of nephrotic syndrome in adults: minimal change disease, focal and segmental glomerulosclerosis, membranous glomerulopathy, membranoproliferative glomerulonephritis, diabetic neuropathy, and amyloidosis. Id. Minimal change disease (MCD) accounts for 20% of nephrotic syndrome in adults. Id.

“The etiology of MCD is unknown and the vast majority of cases are idiopathic.... MCD occasionally develops after upper respiratory tract infection, immunizations, and atopic attacks.” Id. at 1541. An immune etiology is suggested. Id.

The second item in Vol. VIII is an article entitled, “Immune-mediated pathology following hepatitis B vaccination. Two cases of polyarteritis nodosa and one case of pityriasis rosea-like drug eruption,” by F. De Keyser, et al., 18 *Clin & Experimental Rheum* 81-85 (2000). The authors discuss vasculitis reactions to hepatitis B vaccination. In the first case, a 45-year-old man experienced myalgia, joint pain, and morning stiffness two weeks after his first hepatitis B vaccination, and an ulcer in his left lower limb, and an increase in arthralgia and myalgia an unspecified period of time after his second hepatitis B vaccination. In the second case, a 35-year-old nurse experienced fever with myalgia and coughing two weeks after receiving a second hepatitis B vaccination. She kept remitting and relapsing over every two-week interval, together with a skin rash. In the third case, a 38-year-old man had a slight rash after a fifth hepatitis B vaccination. One year after that, he received another hepatitis B vaccination and, two days afterward, developed a rash.

The third item in Vol. VIII is a letter entitled “Glomerulonephritis after recombinant hepatitis B vaccine” by M. Pennesi, et al., 21 *Ped Infectious Dis J* 2:172-73 (2002). They describe a 12-year-old girl who had a sudden onset of hematuria (presence of blood in the urine)⁷ two weeks after receiving her second recombinant hepatitis B vaccination. She had a similar episode two weeks after receiving her first hepatitis B vaccine. This episode was self-limiting. Her renal biopsy showed the presence of hepatitis B surface antigen in renal tissue. Id. at 172. The authors state, “In our case, ... a clear temporal association was present between HBV vaccine administration and the start of

⁷ <http://www.wordreference.com/definition/hematuria.htm?v=b>.

hematuria. In addition a renal biopsy was performed in our patient and demonstrated mesangial proliferative glomerulonephritis with IgA deposits, similar to that described in HBV-related glomerulonephritis. HbsAg was identified in renal tissue and in the tubular and peritubular zones.” Id. at 173. They conclude, “Although it is not possible to prove the causal link between our observation and the immunization, the time link and the presence of the antigen in the renal biopsy are compelling.” Id.

The fourth item in Vol. VIII is a letter entitled “Hepatitis B vaccine side-effect” by Y. Carmeli and R. Oren, 341 *Lancet* 250-51 (Jan. 23, 1993). They describe a 21-year-old man who was admitted to the hospital with periorbital edema that developed gradually over two weeks. His admission to the hospital was six weeks after his third hepatitis B vaccination, making the onset of edema four weeks after vaccination. Id. at 250. The authors believe that his glomerulonephritis was caused by hepatitis B vaccine. Id. at 251.

The fifth item in Vol. VIII is a case report entitled “Large Artery Vasculitis Following Recombinant Hepatitis B Vaccination: 2 Cases” by A. Zaas, et al., 28 *JRheum* 1116-20 (2001) [only pp. 1116-18 were filed]. They describe two women, one 19 years old and the other 61 years old, who developed large artery vasculitis after receiving hepatitis B vaccine. The first woman received hepatitis B vaccinations in March, April, and September 1995, and developed fatigue and malaise in the summer of 1995. In October 1995, she developed severe headaches. The second woman had fatigue, myalgias, and eye pain the night following her first hepatitis B vaccination. After the second vaccination, she rapidly developed fatigue, low grade fevers, anorexia, and headache. Id. at 1116.

Petitioner filed as Vol. IX four items. The first is a letter entitled “Nephrotic syndrome following hepatitis B vaccination” by O. Istek, et al., 14 *Ped Nephrol* 89-90 (2000). This is the same article that petitioner filed as the second item in Vol. V. The second is a case report entitled “Guillain-Barre Syndrome Following Recombinant Hepatitis B Vaccine and Literature Review” by S. Sinsawaiwong and P. Thampanitchawong, 83 *J Med Assoc Thai* 1124-26 (2000). They describe the case of a 17-year-old female admitted to the hospital with progressive weakness for one week. Ten days before admission, she received her first hepatitis B vaccination. Three days after vaccination, she developed headache, fatigue, and weakness. *Id.* at 1124.

The third item in Vol. IX is “Surveillance for Safety After Immunization: Vaccine Adverse Event Reporting System (VAERS)– United States, 1991-2001,” by W. Zhou, et al., 52 *MMWR* SS-1 (Jan. 24, 2003). From 1991-2001, there were inter alia the following reports of symptoms, the number of reports, and their percentage of adverse event reports:

Adverse event	No.	(%)
urine abnormality	223	(0.2)
chest pain	1,752	(1.4)
abdominal pain	2,254	(1.8)
edema	3,504	(2.7)
peripheral edema	4,165	(3.2)

There were no adverse event reports of minimal change disease or nephrotic syndrome from 1991-2001 after immunization. *Id.* at 18-19 (*MMWR* page numbering)..

The fourth item in Vol. X is the package insert from Merck, the manufacturer of recombinant hepatitis B vaccine. Under Adverse Reactions, Merck lists an incidence of less than 1% of vaccinations have resulted in complaints of lightheadedness and abdominal pains. *Id.* at 9. Merck does not list any complaints of minimal change disease or nephrotic syndrome.

Petitioner submitted as Vol. X a “brief report” entitled “Pulmonary Hemorrhage in a Patient with Fibrillary Glomerulonephritis” by R.G. Masson, et al., 326 *New Eng J Med* 36-39 (1992). The authors discuss an unusual kidney disease thought to be mediated by local production or deposition of abnormal paraproteins. They describe a 68-year-old woman who died of respiratory failure 20 hours after admission to the hospital. Id. at 36. Her renal disease was accompanied by recurrent pulmonary hemorrhages. Id. at 37. Alveolar hemorrhage occurs in association with a number of immunologic and idiopathic processes affecting both lungs and kidneys, including Goodpasture’s syndrome, Wegener’s granulomatosis, lupus erythematosus, idiopathic rapidly progressive glomerulonephritis, and vasculitides. Id. at 37-38.

TESTIMONY

Dr. Michael Heifets, petitioner’s former treating nephrologist, testified first for petitioner. Tr. at 10. He stated he is familiar with the immunologic aspects of nephrology. Id. He is now Medical Director of the Kidney and Pancreas-Kidney Transplant Program at Hahnemann University Hospital. Tr. at 11. When Dr. Heifets met petitioner, petitioner was referred to him because of shortness of breath, edema, and fluid overload. Tr. at 12. He had progressive edema, swelling of his lower extremities, progressive shortness of breath, progressive weight gain, generalized aching, and fatigability. Tr. at 13. Petitioner’s onset was progressive. Id. Dr. Heifets was aware the onset was within weeks of petitioner’s visit to the emergency room on December 8, 2000. Tr. at 14. He had nil disease or minimal change disease. Tr. at 26. Dr. Heifets’ recollection is that petitioner’s symptoms were progressive over several weeks. Tr. at 13. It was clearly a recent presentation. Tr. at 22.

Without a biopsy, it is hard to decide what causes nephrotic syndrome. Tr. at 21. Petitioner's onset over months was more consistent with minimal change disease. Tr. at 21-22. Nephrotic syndrome is a combination of significant protein in the urine (more than four grams), complicated by edema, and an increase in lipids (triglycerides and cholesterol). Tr. at 22. The causes relate to a significant loss of protein in the kidney due to damage to the kidney's filters, the glomeruli. Tr. at 23. Immunizations are one cause. Id. Another cause are hepatitis B and C infections. Id. Minimal change disease most commonly responds to steroids and is immune-mediated. Tr. at 24.

After petitioner had a kidney biopsy, he developed peripheral neuropathy and Dr. Heifets recommended he see Dr. David Lee, a neurologist. Tr. at 24-25. Petitioner has a relapsing form of nephrotic syndrome, which is the nature of minimal change disease. Tr. at 25. The biopsy did not yield a cause. Tr. at 26. Initially, petitioner's minimal change disease was steroid-responsive, but he later relapsed. Tr. at 38.

Dr. Heifets opined that the onset of petitioner's nephrotic syndrome was October or early November 2000, or six to eight weeks after vaccination. Tr. at 30-31. This interval is consistent with causation from the second hepatitis B vaccination because it gives time for the formation of antibodies and vaccine particle complexes. Tr. at 31. There is a silent phase while injury is cascading in the immune system, an immune-mediated process injuring the glomeruli in the kidneys. Id. He stated that six weeks is actually a very short time for a disease process to gain speed. Tr. at 32. There are a dozen different causes for minimal change disease, including drugs, allergic reactions, tumors, viral infections, parasitic infections, and immunizations. Tr. at 35.

Dr. Heifets went to the National Library of Medicine database and did an extensive literature search to look at the complications of vaccines in general as well as specifically to hepatitis B

vaccine. Tr. at 40-41. He also reviewed standard nephrology texts, such as by Schrier and Brenner. Some of the case reports are submitted into evidence. Tr. at 41. Dr. Heifets stated Merck's package insert for hepatitis B vaccine contains case reports. Merck, the manufacturer, indicates a number of immune syndromes have been reported with hepatitis B vaccine, including lupus and Stevens-Johnson syndrome, which is an extreme allergy that has been linked to minimal change disease. Tr. at 43. It bothers him that there are no epidemiologic studies. Tr. at 43-44.

Hepatitis B vaccine is made of proteins that serve as antigen to which the body responds by making an antibody. Tr. at 46. The protein that leaks in the kidney in nephrotic syndrome is a different kind of protein (albumin). Tr. at 47. The antibodies are proteins of a different class. Tr. at 48. They have a different shape and size. Id. Petitioner could have had a hypersensitivity reaction. Tr. at 46. The protein in the kidneys that leaks is albumin, a major protein present in the blood. Tr. at 47. Hepatitis B infection causes renal disease and can take any form, most often membranous nephropathy whose onset is usually longer than 6 to 8 weeks. Tr. at 48-49. The second hepatitis B vaccination starts complexing with antibodies in the system, which have to be cleared from circulating in the blood by filtering through the kidneys, passing through the free-floating membrane and through the mesangial cells. Tr/ at 52-53. Even after the complexes have cleared, the lining of the glomeruli leak and the podocytes lift (the foot process). The podocytes are cells with multiple appendages attached to the membrane preventing large molecules such as albumin from passing. Tr. at 53.

The medical literature reports that hepatitis B vaccine causes nephrotic syndrome. Tr. at 54. The Morbidity and Mortality Weekly Report (MMWR) for January 2003 reports cases of proteinuria and hematuria after vaccination. Tr. at 54-55.

Dr. Heifets does not know why petitioner has peripheral neuropathy. Tr. at 56. It is probably related to hypo-albuminemia (drop in the albumin level in the blood), swelling the lower extremities. Tr. at 57. Albumin holds fluid in the blood vessels. Id. When the albumin is low, there is low oncotic pressure, leading to swelling of tissues outside blood vessels where the nerves run, damaging them. Id. Minimal change disease is a dysregulation of the immune system. Tr. at 62.

Dr. Heifets cannot say whether petitioner's first hepatitis B vaccination on August 10, 2000 or his second hepatitis B vaccination on September 13, 2000 caused his minimal change disease. Tr. at 64. He believes the second vaccination is a substantial factor in causing it. Tr. at 64, 71, 72. He stated respondent's expert, Dr. Michael Gottlieb, is a very respected nephrologist and he agrees with him about all the statements he made about nephrotic syndrome in general, but they disagree on the validity of case reporting and the causality of nephrotic syndrome and hepatitis B vaccination in this case. Tr. at 72-73.

On cross-examination, Dr. Heifets admitted that he recorded a history at his first meeting with petitioner on December 14, 2000 of a several week history of symptoms, which would put onset 10-12 weeks after vaccination, not 6-8 weeks. Tr. at 73-74. He responded that the symptoms were there for a long time but petitioner was not noticing them. Tr. at 74. Dr. Heifets said his source for this information is petitioner and his recollection. Id.

Petitioner Thomas Stewart then testified that he had abdominal pains two weeks after his second hepatitis B vaccination and swollen legs five weeks after this vaccination. Tr. at 75-76. When he came home, he had no ankles and called his cousin, who is a nurse. Tr. at 77. She told him to seek medical attention. Id. He got lightheaded and went to the emergency room on December

8, 2000. Id. The suds in his urine were three to four weeks after his second hepatitis B vaccination in early November, and before his legs swelled. Tr. at 78.

Dr. Heifets interpreted “several weeks” to be between 4-10 weeks. Tr. at 81-82. He stated that all vaccines cause immune response. Tr. at 83. Sometimes, he determines the cause of minimal change disease in patients due to drugs or infection. Id. Harrison’s text states the etiology is unknown and most cases are idiopathic. Tr. at 83-84. The case reports in the literature show an onset of a few days to two weeks, not 6-8 weeks. Tr. at 87. Petitioner did not have a fluid overload on December 8, 2000. Tr. at 88. It took time to develop. Id. Merck’s package insert does not list minimal change disease, focal and segmental glomerulosclerosis, or nephrotic syndrome. Tr. at 86.

Dr. Michael N. Gottlieb, a nephrologist who teaches at Harvard Medical School, testified for respondent. Tr. at 95. He has been practicing for 31 years. Id. Minimal change disease is unique. Tr. at 97. It is rarely associated with end-stage renal disease, and rarely manifests with blood in the urine (hematuria). Tr. at 98. Rarely does one identify a cause for minimal change disease. Tr. at 98-99. It is idiopathic. Tr. at 99. It has an immunologic flavor and ought to be immune-mediated because it responds to steroid therapy. Id.

Dr. Gottlieb stated he does not know if petitioner’s peripheral nerve disease is caused by his minimal change disease. Tr. at 100. In nephrotic syndrome, the body thinks it is dehydrated and retains water. Tr. at 103. There are hundreds of millions of hepatitis B vaccinations and only a few case reports of this disease. Tr. at 106. Dr. Gottlieb would like to see either on a biopsy some histologic evidence showing him a relation to hepatitis B vaccine or shown some mediator stimulated by hepatitis B vaccine that induces glomerular injury in order to prove causation. Tr. at 108.

The process Dr. Heifets described of antibodies getting stuck in the kidneys beneath the podocytes is not present in people with minimal change disease. Tr. at 111. Only glomerular diseases that are mediated by antibody-antigen complexes have that type of response. Tr. at 110. In minimal change disease, we do not see extraneous material in the basement membrane, a subcellular structure. Tr. at 111-12. There is no smoking gun in minimal change disease. Tr. at 112. Perhaps there is a chemical cause for minimal change disease which does not deposit anything in the glomerulus, but we do not know that yet. Id. Dr. Gottlieb considers it a leap of faith to say there is a probable causal relationship between hepatitis B vaccine and minimal change disease. Id.

In the case reports, onset was two weeks after vaccination. Tr. at 115. Six to eight weeks is less likely although not impossible. Id. Minimal change disease can remain subclinical for months without any way to know if it occurred. Tr. at 118. There are delayed immunologic reactions from days to weeks, and immediate hypersensitivity reactions (hives, itching, asthma, flushing). Tr. at 114.

Dr. Gottlieb said there is not enough evidence to show that petitioner's hepatitis B vaccination caused his minimal change disease. Tr. at 122. He admitted on cross-examination that he does not know that hepatitis B vaccine did not cause it, and he does not know the cause of petitioner's minimal change disease. Tr. at 129.

Dr. Heifets stated he does not know what petitioner's abdominal pain reflects. Tr. at 133. It could be fluid retention, but it was not persistent. Tr. at 134.

DISCUSSION

Petitioner is proceeding on a theory of causation in fact. To satisfy his burden of proving causation in fact, petitioner must offer "proof of a logical sequence of cause and effect showing that

the vaccination was the reason for the injury. A reputable medical or scientific explanation must support this logical sequence of cause and effect." Grant v. Secretary, HHS, 956 F.2d 1144, 1148 (Fed. Cir. 1992). Agarwsal v. Secretary, HHS, 33 Fed. Cl. 482, 487 (1995); see also Knudsen v. Secretary, HHS, 35 F.3d 543, 548 (Fed. Cir. 1994); Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993).

Without more, "evidence showing an absence of other causes does not meet petitioners' affirmative duty to show actual or legal causation." Grant, supra, 956 F.2d at 1149.

Petitioner must not only show that but for the vaccine he would not have had the injury, but also that the vaccine was a substantial factor in bringing about his injury. Shyface v. Secretary, HHS, 165 F.3d 1344 (Fed. Cir. 1999).

The first issue in this case is one of onset. Petitioner testified that the onset of his symptoms of nephrotic syndrome began within two weeks of his second hepatitis B vaccination, making it late September or early October 2000, but his expert, Dr. Heifets, bases his opinion of causation on an onset interval that goes out to 6-8 weeks, or October or early November 2000. What do the medical records, which include petitioner's history, indicate?

Petitioner first sought medical assistance on December 8, 2000, a little over 12 weeks (or three months) after his second hepatitis B vaccination. Petitioner stated in his second affidavit that, at this time, he thought he was having a heart attack and did not tell anyone in the emergency room of his prior stomach pains or urine froth. However, he did tell the doctors that he had precordial discomfort lasting a couple of hours that started about two and one-half days earlier, or about December 5, 2000. He also told them that, one and one-half days previously, or about December 6, 2000, he had dyspnea, and "tonight" (meaning December 8, 2000), he had swelling of his lower

extremities. He discussed this with his relative who is a nurse and she asked him if he were lightheaded. After he spoke to her, he felt lightheaded.

If one reads petitioner's affidavits and listens to his testimony, the unmistakable impression one has is that the swelling of petitioner's lower extremities occurred weeks, even months, before December 8, 2000, yet the history he gave to medical personnel for the purpose of diagnosis and treatment at the time belies this.

When he was admitted to the hospital on December 9, 2000 to take a stress test, he again had an opportunity to give a history. He said he had noted swelling of his lower extremities over the last several days. Yet, petitioner testified that he had swollen legs five weeks after vaccination, or mid-to late-October 2000, not several days before December 9, 2000. Petitioner told the medical personnel at the hospital that he had no history of similar problems, such as leg swelling in the past. He denied aches and pains.

In answer to questions from a nurse practitioner at the hospital on December 9, 2000, petitioner stated he had no acute or chronic pain. Initially, he had +1 edema bilaterally in his lower extremities, but now it was +2. His edema would increase rapidly over the next week.

By the time he saw Dr. Heifets on December 14, 2000, petitioner could not reasonably have thought he was having a heart attack. Therefore, there would be no excuse for him not to give an accurate history to Dr. Heifets. He told him that he had noted progressive increase in peripheral edema and weight gain over the last several weeks as well as appearance of suds in his urine several weeks ago. One must assume that several weeks does not mean two months. He told Dr. Heifets he had no past history of abnormal urine appearance. Although in the hospital on December 9, 2000,

his edema was +2, it was now +3. He told Dr. Heifets about his two hepatitis B vaccinations. Dr. Heifets was unsure what was the etiology of petitioner's acute onset of nephrotic syndrome.

Well-established case law holds that information in contemporary medical records is more believable than that produced years later at trial. United States v. United States Gypsum Co., 333 U.S. 364, 396 (1948); Burns v. Secretary, HHS, 3 F.3d 415 (Fed. Cir. 1993); Ware v. Secretary, HHS, 28 Fed. Cl. 716, 719 (1993); Estate of Arrowood v. Secretary, HHS, 28 Fed. Cl. 453 (1993); Murphy v. Secretary, HHS, 23 Cl. Ct. 726, 733 (1991), aff'd, 968 F.2d 1226 (Fed. Cir.), cert. denied sub nom. Murphy v. Sullivan, 113 S. Ct. 263 (1992); Montgomery Coca-Cola Bottling Co. v. United States, 615 F.2d 1318, 1328 (1980). Contemporaneous medical records are considered trustworthy because they contain information necessary to make diagnoses and determine appropriate treatment:

Medical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium. These records are also generally contemporaneous to the medical events.

Cucuras v. Secretary, HHS, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

The undersigned holds that petitioner's onset of nephrotic syndrome or minimal change disease was either late November or early December 2000, based on the histories he gave on December 8, 9, and 14, 2000. That means that the next issue is whether hepatitis B vaccine caused the onset of petitioner's nephrotic syndrome two and one-half months later.

On December 14, 2000, Dr. Heifets initially thought the etiology of petitioner's nephrotic syndrome was unclear. By the December 28 to 30, 2000 hospitalization, Dr. Heifets was puzzled (his term) about associating the onset of petitioner's nephrotic syndrome with his recent hepatitis B vaccination. By March 20, 2001, in a letter to petitioner's counsel, Dr. Heifets was willing to state

that, due to temporal association and the lack of any other cause (febrile illness, infection), hepatitis B vaccine “could have” triggered an immune reaction, resulting in protein leak in the kidneys. This is legally insufficient since a temporal relationship by itself cannot form the basis for an opinion of causation, and the lack of other known causes does not provide affirmative proof of causation. (Dr. Steven Klein, who rates disability, similarly opined that hepatitis B vaccine caused petitioner’s nephrotic syndrome and he had no other risk factors. This is equally insufficient legally for the same reasons as stated above.) See, Hasler, supra, and Grant, supra.

By November 18, 2003, Dr. Heifets, in another letter to petitioner’s counsel, stated that, again based on the temporal association, hepatitis B vaccination caused petitioner’s nephrotic syndrome. In another letter, dated January 12, 2004, to petitioner’s counsel, Dr. Heifets stated the onset interval can be weeks or months. The length of time is due to nephrotic syndrome being immunologically mediated, resulting in a “silent immunologic process.” Based on his clinical experience and the medical literature, Dr. Heifets could state “with certainty” that hepatitis B vaccine caused petitioner’s nephrotic syndrome. (One might note that, with this opinion of a silent immunologic process “that takes time to exert substantial damage to the kidney structure,” as Dr. Heifets wrote in his letter to counsel, petitioner’s alleged onset of two weeks would defeat Dr. Heifets’ opinion of causation.).

What does the medical literature upon which Dr. Heifets relies to proffer his opinion contain? In those items which deal with kidney disease following hepatitis B vaccination, the onset intervals are: four days (Vol. V, Ex. 2, first item); eight days (Vol. V, Ex. 2, second item); two weeks (Vol. VIII); and four weeks (Vol. VIII). None of these items would justify an opinion that hepatitis B vaccine causes minimal change disease two and one-half months after vaccination.

In Dr. Heifets' testimony, he also pointed to the Merck package insert as a basis for his opinion, but Merck does not indicate nephrotic syndrome or minimal change disease being reported as an adverse reaction. For that matter, in the years between 1991-2001, the VAERS material published in the MMWR, upon which Dr. Heifets also relied in his testimony, does not mention adverse reaction reports of minimal change disease or nephrotic syndrome.

Both Dr. Heifets and Dr. Gottlieb proffered theories about how hepatitis B vaccine could cause minimal change disease, but that does not help the undersigned find a basis that it did cause it in this case. Dr. Heifets' theory of the deposition of antigen-antibody complexes in the membranes of the kidney was undercut by Dr. Gottlieb's testimony that minimal change disease does not involve the deposition of physical particles in the kidneys. Dr. Gottlieb offered the hypothesis of a chemical reaction as some explanation for the cause of minimal change disease, but it is not proven. Possibility is not the legal standard which underlies petitioner's burden of proof. Probability is the standard. Dr. Heifets' opinion that hepatitis B vaccine probably caused petitioner's minimal change disease is not credible because his opinion contradicts the medical literature upon which he supposedly relies as well as the physiologic process underlying minimal change disease as Dr. Gottlieb described it.

The undersigned has previously ruled that hepatitis B vaccine caused in fact petitioner's focal segmental glomerulosclerosis (FSGS), a form of nephrotic syndrome. Larive v. Secretary of HHS, No. 99-429V, 2004 WL 1212142 (Fed. Cl. Spec. Mstr. May 12, 2004). In Larive, petitioner developed edema one month after his second hepatitis B vaccination, and edema, vomiting, and nausea one week after his second hepatitis B vaccination (as well as edema one to three weeks after an upper respiratory infection and severe edema one month after MMR vaccine). The undersigned

held that hepatitis B vaccine caused his FSGS based on the rechallenge from his third hepatitis B vaccination, plus the one-month's interval being an appropriate time for a triggering factor to provoke his edema and other symptoms (both parties' expert doctors agreed that the one-month interval was appropriate for this type of reaction).

In the instant action, the undersigned would have accept that two and one-half months is an appropriate time for causation, even though nothing in the medical literature supports this. That there is no other cause apparent is not sufficient to satisfy petitioner's burden of proof. Grant, supra.

Dr. Heifets' transformation from having no idea what the cause of petitioner's nephrotic syndrome is (his early medical records) to having certainty that hepatitis B vaccine is the cause does not bode well for credibility. His study of the Merck package insert, the MMWR, and the case reports would not lead to certainty, much less probability, that hepatitis B vaccine causes minimal change disease two and one-half months later. All he really has for a basis for his opinion is an immunologic theory that Dr. Gottlieb, for whom Dr. Heifets has great respect, has disproven as unrelated to minimal change disease. That is insufficient to satisfy petitioner's burden. Petitioner has failed to prove a prima facie case that hepatitis B vaccine caused in fact his nephrotic syndrome or minimal change disease. The undersigned must dismiss his petition.

CONCLUSION

This case is dismissed with prejudice. In the absence of a motion for review filed pursuant to RCFC Appendix B, the clerk of the court is directed to enter judgment in accordance herewith.

IT IS SO ORDERED.

DATE

Laura D. Millman
Special Master